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BACILLUS NECROPHORUS AND ITS ECONOMIC IMPORTANCE.

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BACILLUS NECROPHORUS AND ITS ECONOMIC IMPORTANCE.

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The bacillus of necrosis presents itself as an attractive study because of its ubiquitous character, its highly infectious nature, its extensive range of pathogenesis, the definite form of lesion produced by it, its easy demonstration in those lesions, and the difficulty with which it is isolated. Its interesting character, its economic importance, and the scant literature in English concerning it are the reasons for this study of it.

SYNONYMY.

The following names have been applied to this microorganism: *Bacillus der Kälberdiphtherie* (Löffler), 1884; *Bacillus diphtheriæ vitulorum* (Löffler), 1886; *Bacillus necrophorus* (Flügge), 1886; *Bacillus filiformis* (Schütz), 1887; *Nekrosebacillus* (Bang), 1890; *Streptothrix cuniculi* (Schmorl), 1891; *Actinomyces cuniculi* (Gasperini), 1892; *Bacillus necroseos* (Salomonsen), 1894; *Bacillus des Kälbernoma* (Ritter), 1895; and *Streptothrix necrophora* (Kitt), 1899.

The most careful scrutiny by us of all phases of its morphology having thus far failed to reveal true branching in the necrosis bacillus, we are compelled to regard it as belonging to the Bacteriaceæ and to acknowledge Flügge's priority by calling it *Bacillus necrophorus.*[a]

HISTORY.

To Löffler belongs the credit of discovering, describing, and demonstrating the necrosis bacillus in its relation to the pathologic process whose name it bears. Yet the names of two, and possibly of three, observers may be mentioned by way of introduction.

[a] Lignières and Spitz[20] (see bibliography, p. 113), in their recently published classification of the Actinomyces, confirm our position by removing from the group of Streptothrix and of Actinomyces "microbes like the bacillus of necrosis (improperly *Streptothrix cuniculi*), which do not belong at all to this group."

Dammann [4a] was probably the first to see, Koch the first to note, and Löffler the first to investigate this microorganism. In November, 1876, Dammann published the results of his investigations of a caseo-necrotic inflammation of the mouth, throat, and upper air passages of some sucking calves on a farm in Ludwigsburg, on the shores of the Baltic. The macroscopic lesions closely simulated those found in diphtheria of man; and, since the microscopic examination of those lesions showed the superficial layers crowded with micrococci, which organisms were recovered in great numbers from the blood of the heart of the dead calves and from rabbits inoculated with bits of the diseased tissue, accepting the then prevailing dictum of Eberth, "without micrococci no diphtheria," Dammann pronounced the disease in question diphtheria of calves and regarded it as identical with the disease of the same name in man. However, there can be no doubt that Dammann saw, but failed to recognize, the real cause of the disease in question. On page 12 of his paper, after having described the superficial layers of the pseudomembranous deposits as composed largely of heaps of micrococci, he refers to the middle and deeper layers containing a thick network of fine fibrin threads. His further delineation of these thread forms compels the impression that he was describing the filaments of *B. necrophorus*. Unfortunately, in spite of his carefully reported clinical and postmortem findings, Dammann's work on calf diphtheria can not be safely resorted to for an exact description of the effects of the necrosis bacillus, for the reason that in all his cases he had to do, beyond question, with a complicating septicemia, the result of a virulent micrococcus infection.

It is not without interest to note that in 1878 Feldmann reported a case of diphtheritis in a calf, described symptoms analogous to those in the Dammann calves, and regarded the cases identical. His bacteriologic examination revealed "kugel-und rosenkranzförmige bakterien." While it is true that "rozenkranzförmig" is used in bacteriologic parlance to denote the wavy chains of streptococci, still one who has examined the diseased tissues in necrotic stomatitis in calves will very likely be disposed to translate "spherical and beaded bacteria" and recall how often the beaded necrosis bacillus resembles the undulating chains of streptococci.

Koch, in his work "Zur Untersuchungen der pathogenen Organismen," introduces two microphotographs (Nos. 47 and 48) as "sections from the cornea of a case of sheeppox showing the border of the corneal layer. The ulcerated spot is surrounded by a large nuclear accumulation, and between the nuclei there is diffused a thick felt of bent bacilli, slightly curved, sometimes undulating. At many

[a] The figures refer to the bibliography at the end of this article.

points the bacillary masses advance in front of the nuclei in the still intact corneal tissue, as on No. 47. It is on that account also probable that the ulceration is limited by the immigration of the bacilli. Here and there the bacilli have a granulated appearance—No. 48."

In 1884 Löffler published the results of his now monumental work in diphtheria. In this connection he investigated the so-called "calf diphtheria" of Dammann. On the edges of the caseonecrotic patches Löffler discovered great bundles of *B. necrophorus* and succeeded in conclusively proving their causative relation to the disease in question, on which account he speaks of it as the bacillus of calf diphtheria. In his report Löffler, having noticed the above statement by Koch, says:

> They [the bacilli depicted by Koch] simulate so completely in structure, size, and arrangement those found by me in calf diphtheria that one may be inclined to consider them identical.

And C. O. Jensen, who has, with Bang, made extensive studies with the necrosis bacillus, says of these same Koch bacilli:

> welche so grosse Aehnlichkeit mit Nekrosebazillen darbieten das ihre Identität mit diesem wohl-keinen Zweifel erleiden kann.

Löffler in his report refers to Dammann's success in transmitting the disease from calves to lambs, and states, furthermore, that there occurs among lambs an exceedingly pernicious diphtheria, which, according to the description, bears a great resemblance to that of calves. Querying if the two diseases might not own the same etiologic agent, he quotes Koch's above-mentioned observation to show that a practically identical microorganism does grow in the body of the sheep.

That he did not assert the identity of the two microorganisms is seen by his next paragraph:

> In experiments looking to the transmission of syphilitic products to rabbits I learned to recognize still a third form of bacillus, which morphologically was very similar to that of calf diphtheria.

Then follows the account of a very marked caseonecrotic process, followed by death, induced by these experiments, in which the pathologic picture and bacteriologic factor presented a striking likeness to those of calf diphtheria inoculations.

The effect of this lack of absolute certainty as to the identity of these microbes is seen in the synonymy. In 1886 Flügge describes *Bacillus diphtheriæ vitulorum* as the bacillus of calf diphtheria and *Bacillus necrophorus* as the organism responsible for the caseous necrosis produced by inoculating bits of broad condyloma into the anterior chamber of the eye of rabbits.

In 1887 Bang and Schütz investigated conjointly a severe epidemic of hog cholera in Denmark which was known there largely as swine

diphtheria. Bang, finding that he could kill hogs by feeding pure cultures of the short, ovoid, and motile bacillus discovered by him in the tissues of diseased hogs, attributed also to this bacillus the cheesy necrosis—so-called diphtheritic patches—which appeared to be such a marked characteristics of this disease. On the other hand, Schütz [35] found in the caseous inflammations of the intestines long thread-shaped bacilli which he named *Bacillus filiformis*. He considered the deeply penetrating intestinal necrosis, which he named diphtheritis profunda, analogous to the tissue alterations induced in the mouth by the calf diphtheria germ and expressed the supposition that his *B. filiformis* was identical with that microorganism and was the cause of all the caseonecrotic lesions occurring in hog cholera.

In 1888, Schütz refers to finding similar bacillary forms as the cause of abscesses frequently occurring in the liver of cattle. He performed on rabbits inoculation experiments similar to those undertaken by Löffler, and with like results.

In 1889, Th. Smith [39] reported that—

> In sections of ulcers hog cholera bacilli have been searched for, but the examination of a large number of ulcers showed that no positive results could be obtained. Different ulcers showed different bacteria, sometimes large colonies of micrococci, *sometimes groups of large bacilli, following the course of the blood vessels in the embryonic tissue under the slough.* These no doubt found their way in from the superficial slough which seemed to be made up almost entirely of bacteria.

The italicized portion of Smith's statement is quoted by Jensen in support of the latter's assertion that Smith had seen and described in the intestinal necroses of hog cholera bacillary forms that were identical with *B. necrophorus.*

It remained for Bang to establish the identity of Löffler's two bacteria, Schütz's *B. filiformis*, and the long bacilli of Smith. This he did as the result of a series of observations and experiments reported in 1890. Moreover, by these experiments Bang not only demonstrated the wide scope of its pathogenic influence, as including calves and adult cattle, horses, and hogs among the domestic animals and kangaroos among wild animals, though in a state of captivity, but also recognized the essential feature of its action as a local cheesy necrosis frequently followed by embolic necroses. He therefore gave it the name of Nekrosebazillus, or necrosis bacillus, which idea, however, had been already adopted in Flügge's appellation of *B. necrophorus.*

Acting upon Schütz's hypothesis above mentioned, Bang [13] inoculated mice and rabbits with material from necrotic foci in the intestines of hogs affected with hog cholera and obtained the same lesions at the inoculation point and in the internal organs as those observed

and discovered by Löffler in his calf diphtheria experiments. Thus was verified the suggestion offered by Schütz in 1887.

In 1891 Schmorl reported a most fatal enzootic occurring the previous year among his laboratory rabbits. From the caseonecrotic lesions of those dying he isolated a thread bacterium which, morphologically and biologically, he quite thoroughly studied. Although he named it (believing that he recognized branching) *Streptothrix cuniculi*, it has been identified with *B. necrophorus*.

Through the observations of McFadyean, Kitt, Olt, Jensen, Johne and Schlegel, Horne, and others, the list of animals susceptible to the morbid influence of the necrosis bacillus has been enlarged until it includes aves as well as mammalia; not only domestic animals, but also wild animals, both free and in captivity.

For the determination of the morphologic and biologic characters of the bacillus of necrosis attention is called chiefly to Bang,[1] Schmorl,[38] and Ernst.[10]

OCCURRENCE IN NATURE.

There is hardly room to doubt that *B. necrophorus* is a normal inhabitant of the healthy intestine of at least one species of our domestic animals—hogs—and possibly of the cow and horse. It is also found in the manure, and therefore in soil contaminated with the latter. Bang's discovery of the association of the organism with the necrotic processes in the intestine in hog cholera, and also as cause of an intestinal diphtheritis in calves secondary to an intestinal catarrh, seemed to require the intestine as the normal habitat of *B. necrophorus*. Could this be demonstrated we should then have an explanation of the remarkably ubiquitous character of the organism as exhibited in the wide diversity of diseases caused by it. In this manner could be explained its relation not only to the necrotic inflammations occurring in the vagina and uterus, but also to all the external necrotic processes. This Bang succeeded in doing. He twice made inoculations of the intestinal contents of healthy hogs with the result of demonstrating the presence of *B. necrophorus*. An analogous investigation by him of the intestinal canal of a cow was not so successful.

MORPHOLOGY.

B. necrophorus is essentially a pleomorphic organism. It varies, according to nutrient soil and age of culture, from coccoid forms to filaments over 100 μ in length and from 0.75 μ to 1.5 μ in width. The longer forms appear as slender, undulating, beaded filaments. Generally, in the tissues these threads are matted together into an intricate network, like a mass of hair or even more compact felt. The

same appearance may be found in colonies. Frequently the filamentous forms present one wide or clubbed extremity, with the other extremity tapering. On the other hand, the older cultures—either animal tissues or artificial media—exhibit almost exclusively bacillary forms of various lengths, some so short as to be easily mistaken for cocci. Involution forms may be present in any culture, but certain media, notably that composed of a mixture of agar, gelatin, bouillon, peptone, and salt are particularly favorable to their development.

MOTILITY.

Motion has not been observed in our experiments; in fact, it has been reported by Schmorl only. He examined the pleural exudate in hanging drop.

In this laboratory the examination for motility was made with fresh cultures and with tissue from animals within one hour after death, both by means of hanging drop and by the application of flagella stains. In no case was it possible to claim motion for these bacilli.

STAINING.

The necrosis bacillus stains readily with the ordinary anilin dyes, Löffler's methylene blue, and Ziehl's carbol fuchsin, producing particularly good effects. Alkaline toluidin blue (1 per cent solution), while not giving the brilliant effects of fuchsin, makes perhaps the best reagent for routine use. The slide, or cover slip, dipped in the stain, immediately washed in water and mounted, is a very rapid and satisfactory method of bringing out the beaded appearance of the organism. It does not take Gram's stain.

In the study of fresh tissue smears, it is usually sufficient to make a film on a slide with a teased particle of the suspected tissue, and after the usual preliminaries stain with one of the ordinary dyes mentioned, preferably methylene blue or toluidin blue. Whenever it was desired to employ differential staining, we found the following procedure to answer all requirements: The stains are kept ready for use in wide-mouthed bottles. Prepare the film on the slide in the usual manner, fix in the flame, dip from two to five seconds in a 1 per cent alkaline toluidin blue, wash thoroughly in water, counterstain in a 0.2 per cent Neisser's Vesuvian brown, finally wash in water, dry, and then mount in balsam.

Mention has been made of the beaded appearance of *B. necrophorus* in stained preparations. This is noticeable equally in tissue smears or sections and in films from cultures. The longer rods and threads particularly exhibit this characteristic. It is due to the occurrence

in the filaments of unstained spaces which were at first thought to be spores. Spore-staining methods, however, do not alter them. Careful study of this peculiarity reveals several phases of it. Sometimes a thread will be most regularly marked off into alternate sections of stained and unstained material; again, decided irregularity characterizes the arrangement—long vacuole-like inclusions alternating with shorter stained squares or bacillus-like spaces of stained material may alternate with shorter colorless portions; again, the vacuoles may appear like a chain of colorless rods lying on a ribbon of blue or whatever color may be used for the stain. Sometimes the stained material is so little in quantity that the thread seems like a string of spores, oval or rod shaped, with thin, deeply stained partitions between them. On the other hand, the filament presents itself as an unstained tube with a regular succession of deeply stained coccus-like granules much resembling streptococci, or these granules may be alternately arranged along the sides of the tube.

BIOLOGY.

Cultivation of *B. necrophorus* is not easy. It is an absolute anærobe. Investigators differ concerning its requirements as to temperature. Nocard and Leclainche give 30° to 40° C. as the limits of growth, with the optimum at 37° C.; Jensen adopts the same extremes, but places the optimum at 34° C.; whereas, according to Ernst, development occurs only between 36° and 40° C., and the optimum is 39° C. Our own investigations have shown that 30° to 40° C. represent the extremes of temperature at which the ordinary work of the laboratory may be satisfactorily carried on; nevertheless, we have on different occasions been able at 28° C. to grow in agar-bouillon shakes typical colonies, which responded to the usual tests of morphology, odor, and pathogenesis. With us the optimum was 35° C.

The usual culture media of the laboratory are either unsatisfactory for the development of the necrosis bacillus or altogether inimical to it. Agar-agar was often employed with only passable results, but more satisfaction was obtained from the following combinations: Agar-bouillon (A–B), agar-gelatin (A–G), serum-agar (S–A), serum-agar-gelatin (S–A–G), and two suggested by Ernst—1.5 per cent agar in a peptone-salt-bouillon (A–B–P–S) and 0.7 per cent agar and 7 per cent gelatin in bouillon with 5 per cent peptone and 2.5 per cent salt (A–G–B–P–S). The first four mixtures were usually prepared in the proportions of equal parts, although other proportions were adopted for the purpose of varying the consistency of the medium. Fluid blood serum, milk, rabbit bouillon, and Martin's bouillon were also employed.

PLATE CULTURES.

Bouillon-agar.—Great difficulty was experienced in getting the organism to develop colonies in Petri dishes. Numerous attempts were made by displacing air with hydrogen in a hydrogen jar, and by the formation of a vacuum by withdrawing the air under a bell jar by means of a vacuum pump, but success was not attained in any instance. Recently it was endeavored to grow the organism in Petri dishes placed in a closed jar containing a solution of pyrogallic acid rendered alkaline by sodium hydrate. This method, which permitted the presence of only the inert nitrogen gas, finally resulted in characteristic colonies occurring throughout the medium with the formation of numerous gas bubbles. Several of these colonies in the dish of the second dilution grew so close to the surface that some filaments extended to the upper stratum and could be removed by means of a platinum needle. In about forty-eight hours after exposing the plates to this method, small, pinhead-sized, dirty-white, opaque, round colonies, possessing no distinctive features, were visible to the unaided eye below the surface. Many small round or oval gas bubbles could also be observed. By means of a small magnifying glass these colonies were seen to possess a yellowish-brown center surrounded by a thin, light, almost translucent border, which, under the microscope, appeared floccose. After three days the colony presented to the naked eye a woolly appearance, and the microscope now revealed the central structure as a felted maze of threads and the floccose character of the border as long, wavy filaments.

SHAKE CULTURES.

Agar-bouillon.—In eighteen to twenty-four hours after inoculating a tube either from necrosed tissue or from a colony in another tube, or with a loopful from the depths of a pure Martin's bouillon culture, the tube is studded with small oval gas bubbles. At this time, also, rarely with the A–B medium, frequently with the softer forms, as S–A–G, A–G (2:1), A–B–P–S, and A–G–B–P–S, the column of culture medium will be transversely ruptured in one, two, or more places by the pressure of the gas. In forty-eight hours these sections will often be separated 2 to 5 mm. and even more from each other. We have sometimes seen this gas formation go on for the next two days energetically enough to raise the upper portion of the medium 2 cm. The dilution from the above-described tube—tube 2—would often follow tube 1 quite closely in the quantity of gas bubbles formed, though not in the breaking up of the medium. Tubes 3 and 4 would usually show a great diminution in the quantity of gas bubbles and no breaking up of the medium.

In the development of the growth our experience tallied quite closely in a few notable points with that of Ernst. For instance, shakes sown with necrosed material would often show, after thirty-six to forty-eight hours, a fine grayish-white mist of cloudiness at the lower portion of the tube. In our experience, even with slight magnification, it was possible to detect no particular structure. A film made from this portion of the culture medium would always show beaded forms. Again, when the medium used was jelly-like in consistency, the unabsorbed gas, instead of remaining as bubbles at the point formed, would gradually float upward toward the surface. The original seats of these bubbles and the pathways along which they had risen would be coated with a fine bacterial growth. Thus would be formed numerous filmy ribbons, extending from near the surface down into the depths of the tube, where they would be anchored by a crescent-shaped body. The time and rate of growth and appearance of colonies in the tube are sufficiently described in the above description of plates.

STAB CULTURES.

Agar-agar.—Near the close of the second day a few grayish-white colonies make their appearance at the bottom of the needle track. Gradually these increase from below upward to within 1–1.5 cm. of the top of the stab canal. Thus is formed a thin, narrow, opaque, yellowish or grayish-white line of growth surrounded by a thin whitish cloud, which on slight magnification is seen to be composed of minute wavy threads.

Serum-agar.—Time and height of bacterial growth and gas formation are like the preceding. At times the needle track is the center of a whitish film or merely a thin line of cloudiness of the medium; again, the growth may be denser, similar to that described for agar-agar. The serum is never liquefied, although in very old cultures it will be natural that the zone of cloudiness referred to will have spread nearly to the walls of the tube.

CULTURES IN FLUID MEDIA.

Bouillon.—The organism can be grown in ordinary peptonized beef broth, rabbit bouillon, and in Martin's broth, the maximum development occurring at the temperature of 35° C. in a hydrogen jar. The bouillon becomes turbid with the formation of some gas, which is noticeable by the surface bubbles. Later the bacillary masses sink to the bottom in the form of whitish, viscid flakes, causing the fluid to become clearer. The cultures have a peculiar odor, very characteristic, which will be referred to later. There is no film formation, but a tendency to develop a ring around the border of the medium has been observed.

ACTION OF GERMICIDES.

In determining the germicidal power of disinfectants a measured volume of a forty-eight hour bouillon culture of the necrosis bacillus was intimately mixed with an equal volume of the disinfecting solution, thereby reducing the strength of the germicide to one-half. Three platinum-wire loopfuls were then transferred to fresh rabbit bouillon tubes after varying periods of exposure. After an exposure of one minute in a 2 per cent solution of carbolic acid the bouillon tubes showed growth, but in the tube representing a two-minute exposure no development occurred. With bichloride of mercury an exposure of 9 minutes to a $\frac{1}{2000}$ solution prevented growth. Formalin in the strength of $2\frac{1}{2}$ per cent solution (1 per cent formaldehyde) killed the organism in thirteen minutes.

CHEMICAL ACTIVITIES.

PIGMENT PRODUCTION.

Chromogenesis is wanting.

ODOR PRODUCTION.

All cultures develop a substance or substances which emit an odor well described by Ernst as between the odor of cheese and that of glue. The stench is so characteristic that the presence of the bacillus is recognized at once in the tissues of either natural or experimental infection as well as in cultures on artificial media.

PRODUCTION OF SUBSTANCES THAT LIQUEFY.

Gelatin is not liquefied. The growth of the bacillus is likewise without effect on blood serum.

INDOL FORMATION.

Indol is formed and may be demonstrated in three-day-old cultures made in Martin's bouillon.

PRODUCTION OF CURDLING FERMENTS.

Milk is not coagulated nor is acid produced. Fluid serum is coagulated.

PRODUCTION OF TOXINS.

That the necrosis bacillus produces a toxin is evidenced, not by the isolation of the same from artificial cultures, but by (1) the character of death in the disease, (2) the quality of the rigor mortis, and (3) the study of the pathologic histology.

The toxic character of death is not particularly noticed in animals suffering from stomatitis when inappetency and inability to take nourishment have produced an enfeebled condition. Nor, again, is it noticeable in those animals which die with embolic foci in liver or lungs, the symptoms arising from the diseased organs often masking the signs of intoxication. However, rabbits inoculated subcutaneously in the back will persist, without any other sign of the disease except the abscess, for about five or six days. Suddenly, on the sixth or seventh day, without any premonitory signs, the rabbit will be thrown into convulsions, coming out of one to lie with its head turned sideways and buried in the bottom of the cage until another attack, dying usually in a few hours after the first convulsion. Quite often in these cases the local lesions will not be sufficient to produce death directly, not being very extensive and not involving any important organ. Such a course as this points unmistakably to a toxinemia which has attacked the nervous system.

The limits of this article do not permit a discussion of the factors entering into the production of cadaveric rigidity. For our present purpose it is sufficient to call attention to the fact that the intensity and long duration of the rigor mortis observed in the experiment animals and described later in this paper comports perfectly with the well-known fact that the presence of toxins in the blood promotes muscular rigidity.

It may be stated with positiveness that *B. necrophorus* does not enter an unimpaired tissue. Most, if not all, of its infections with which we are acquainted require for their inception a break in the continuity either of mucous membrane or skin. A histologic study of an affected area, elsewhere examined in greater detail, reveals a center of completely destroyed tissue marked by an entire absence of the specific bacteria in question. The boundary of this dead area is formed by great bundles of filaments of *B. necrophorus*, large numbers of leucocytes, and a fair sprinkling of tissue cells whose nuclei still respond to stains. The immediately adjoining border of surrounding healthy tissue is seen when carefully examined to possess numerous cells whose protoplasm has been more or less destroyed, and in among these dying cells a few scattered filaments have advanced like skirmishing parties before the main army. It is a true picture of a bacillary invasion of tissue begun by means of the noxious effects of a soluble toxin.

Thus far all attempts to recover the toxic substance either from cultures or the bacilli themselves have failed. From this, Jensen, whose assistant, L. Bahr, has made the only experiments thus far recorded, assumes that either the necrosis bacillus forms these substances only in the living animal or they are of such volatile character that they are destroyed as quickly as they are formed.

IMMUNITY.

The literature on *B. necrophorus* has contained no word on acquired immunity until the article by C. O. Jensen referred to above. This eminent investigator and early worker with the necrosis bacillus states that his assistant, Bahr, has demonstrated by experiments not yet published that intravenous injections of cultures of *B. necrophorus* carefully given to goats protect them from quite large quantities of the same given subcutaneously. Jensen further states that Bahr has produced in the same manner an immunity in guinea pigs from intraperitoneal injections. In view of the fact that most investigators pronounce the guinea pig almost if not absolutely immune, the statement needs further elucidation. On the contrary, while we are not willing yet to build any hypothesis upon it, we find that our reinoculation experiments have given us the impression that susceptibility is increased thereby rather than diminished.

PATHOGENIC CHARACTERISTICS.

Under this head we may view the disease-producing power of *B. necrophorus* in four directions. We may consider, first, the character of its pathogenic action—in other words, its general pathology; secondly, the animals susceptible to its morbific influence—its comparative pathology; thirdly, its special pathology, or the different tissues of the animal body which may be affected by its destructive properties; and, fourthly, its experimental pathology, which exhibits those peculiar results, after inoculation in laboratory animals, which form as definite and certain ground of diagnosis as inoculation of culture media or microscopic examination.

GENERAL PATHOLOGY.

This may be broadly stated as a coagulation necrosis with subsequent caseation, characterized by a most malignant tendency to involve the whole organism. This is manifested in three ways—by a progressive advance into the surrounding (especially the deeper) tissues, by an invasion of distant parts of the body by embolic metastasis, and, finally, by general intoxication.

PATHOLOGIC ANATOMY.

The local lesion, primary or secondary, may be described as a sharply circumscribed patch of yellowish or dull brown, sometimes greenish-white, homogeneous, structureless, dry, crumbly tissue débris of soft, cheesy consistency, resembling compressed yeast, and manifesting a characteristic stench that might be described as a com-

pound of the odors of old cheese and glue. The line of demarcation between the living tissue and the dead mass is a narrow hyperemic zone.

PATHOLOGIC HISTOLOGY.

Microscopic examination of the process in its various manifestations reveals always the same picture. It is composed of three zones. The central zone or area of necrosis contains the structureless remains of nuclear and tissue degeneration which show no staining reaction. The periphery of the necrotic area, as brought out by stains, reveals a salient border made up of bundled bacillary filaments mingled with round cells and leucocytes, whereas the central zone contains few or no bacilli. Between the border and the living tissue is a narrow, poorly stained ribbon of necrotic tissue showing but few bacilli.

PATHOLOGIC PHYSIOLOGY.

Necrobacillosis is always an inoculation disease—that is to say, the necrosis bacillus requires for its entrance into the body an impaired tissue; for the skin necrosis, any of the many likely breaks in the cutaneous surface, pressure of harness, burns, sores of any kind; for the hoof necrosis, tread, punctured wounds, suppurating corns, etc.; for necrotic stomatitis, eruption or shedding of teeth, penetration of the mucous membrane by a sharp-pointed particle of food; for necrosis of the genital tract, even the slight abrasions of the mucous membrane common in normal, easy labor, may become the means of infection. At the point of entrance the system recognizes the presence and multiplication of the bacilli by a reaction marked by congestion and reddening, followed by an exudation rich in albuminoids or fibrin-forming substances, and a defensive immigration of leucocytes.

The metabolic products of the bacilli are exceedingly poisonous, killing everything with which they come in contact. Hence the first effect of the organism is a necrosis, or death, of the superficial layer of tissue cells and leucocytes at the seat of invasion. The cells either suffer fragmentation of their nuclei or become transformed into irregular flaky masses—the so-called hyaline masses. This constitutes superficial erosion of the tissue. The process never stops here, though we may often recognize this stage in numerous recent foci of necrosis in a rapidly spreading form of the disease.

The second alteration is the production of false membrane by a combination of coincident changes. On the one hand, the necrosed tissue elements, having lost their nuclei and finer structure, are deprived of their normal granulation and striation and take on a scaly appearance, being converted into hyaline substance; on the other

hand, the albuminous exudate in which these dead cells are bathed precipitates fibrin or coagulates into fine threads. This is known as coagulation necrosis. There is thus formed a false membrane, the result of coagulation necrosis of the inflammatory exudate and the entanglement in its meshes of the hyaline degenerated tissue cells and leucocytes. This gives a grayish compact mass, more or less adherent to the underlying tissue which, by failure of the dead cells to be thrown off, may be built up an eighth of an inch or so.

The third alteration connected with this process is due to an invasion of the deeper tissues. The bacilli are always found on the border line between the living and dead tissue. Here, in great bundles of beaded filaments, they may be seen attacking the healthy tissue, which in turn has erected against the attack a wall of leucocytes, while masses of micrococci, tangles of streptococci, and clumps of bacteria are lodged in the superficial layers. Thus the process is carried down into the deeper tissues, forming ulcers and fistulous tracts of varying depth. By the coagulation necrosis occurring in the region of the blood vessels they become obstructed by pressure or sometimes by thrombosis, and thus the dead tissue becomes avascular, and the necrotic mass undergoes pulverization into finer and minuter particles until it is a dry, crumbly, yellowish mass of tissue detritus resembling cheese.

COMPARATIVE PATHOLOGY.

A brief survey of this field forms an interesting portion of the study of *B. necrophorus* and should prove convenient for reference. Extensive as are the present known boundaries of this field, there can be no question as to further clinical observation including additional forms within the range of the pathogenesis of this bacillus. In fact, since this statement was first penned there have come to our hand two additional species—one a European kite, or glede (*Milvus ictinus*), brought to this laboratory for necropsy; the other the common guinea pig, two animals being sent alive to us from the National Zoological Park. The necropsy of the kite revealed the lesions of avian diphtheria and the necrosis bacillus in great abundance. The two guinea pigs were suffering with submaxillary abscess, identical in origin. The pus from each abscess contained masses of beaded filaments in association with a micrococcus. The filaments isolated from each species responded fully to all the required tests. The animals affected under natural conditions are, as thus far reported, cattle, sheep, goats, antelope, reindeer, red deer, roe deer, horses, asses, hogs, kangaroos, rabbits, dogs, chickens, kite, and guinea pigs. Experimental work has added to the foregoing list mice and pigeons.

SPECIAL PATHOLOGY.

Lodgment in the tissues of the body of a susceptible animal is all *B. necrophorus* requires. Once this is secured where it may develop and throw out its deadly, volatile toxin, all tissues with which it comes in contact become alike a prey to its necrosing action. In spite of numerous overlappings we shall be able to consider this subject in the following order: Necroses of the skin, muscle, hoof, cartilage, bone, mucous membranes (mouth and upper air passages, digestive tract, genital tract), navel, and viscera.

NECROBACILLOSIS OF THE SKIN.

The inflammatory diseases of the skin may for our purposes be classified as (1) erythema, or simple redness of the skin; (2) the eczemas, which may be arranged in five stages—(*a*) the erythematous, (*b*) papular, (*c*) vesicular, (*d*) pustular, (*e*) squamous, this last often passing into a chronic state and giving rise sometimes to the verrucous, or warty, variety; (3) necrotic or gangrenous dermatitis.

Necrotic dermatitis.—Necrotic inflammation of the skin, dermatitis gangrænosa, Haut-brand, or Haut-nekrose of the Germans, are the titles of a group of destructive inflammations of the skin arising from various causes, such as burning, freezing, slight cauterization, trauma, blows, pressure of harness, etc., decubital disease processes in the skin during general infections, embolism, thrombosis, as also from specific infections of the skin. Under this last etiologic factor occur those lesions of the skin caused by the presence of *B. necrophorus.*

Fröhner [11] observed an enzootic of this disease on a large horse farm in Berlin. The affection took the form of multiple necrosis of the skin, the portions implicated being those spots exposed to irritation by the harness, especially the shoulder and sacral regions, the cheeks, and the corners of the mouth. The infection was of a quite malignant character, showing a tendency, in spite of the ordinary antiseptics, to spread and involve the deeper tissues. The necrotic lesions were characterized by the presence of a grayish-yellow, greasy, foul-smelling secretion. In one case the affection began at the left corner of the mouth following injury by the pressure of the head harness. In spite of the application of formalin, the necrosis spread until the entire left side of the head was swollen, with new foci of necrosis making their appearance. Energetic disinfection with creolin water and application of tincture of iodine was always the treatment that succeeded after the milder applications failed. Fröhner considers *B. necrophorus* to have been the infectious agent, operating secondarily at the sites of pressure irritation.

W. R. Davis [6] recognized the connection between very low temperatures and the development of gangrenous dermatitis, admitting the

possibility of the tissues that have been damaged by the effect of cold being invaded by the "ever-present bacillus of necrosis." The cases cited by him, with one death, were affected by working in irritating mud and then at night having the hose turned on the legs and allowed to dry in a cold, drafty stable. As indicative of infection, he emphasizes the intensity of the inflammatory process, the rapidity with which the changes were produced, and the general symptoms—inappetence, rapid and feeble pulse, shivering, high temperature, great depression and weakness, suggesting intoxication. Cases reported by this author [5] in 1897 have a close resemblance to those in his later report, all being included in the form of dermatitis described in the next paragraph.

Necrotic scratches.—Scratches in the horse is essentially a dermatitis, or inflammation of the skin, of that region of the foot known as the fold of the pastern. The affection is also popularly spoken of as grease, greasy heels, etc. Four varieties of scratches may be described, as follows:

(1) An erythematous form, or simple reddening or erythema of the skin.

(2) An eczematous variety, characterized by swelling, reddening, and an exudation. This is the variety most often noticed, and, on account of the exudation, the one that gives rise to the name "grease," or "greasy heels." The erythema, perhaps, frequently occurs without attracting any attention. The dermatitis eczematosa is usually noticed on account of the lameness on beginning to move. If the animal is not allowed to rest, the combined effect of activity and dirt is seen in the further course of the disease in the production of cracks and fissures. There can be no doubt in these cases as to the frequent presence of some infection superadded to the primary causes of irritation, such as sand, dirt, and even chemical irritants.

(3) A third variety of scratches is that which constitutes what is commonly known as grapes. It is the so-called verrucous scratches. This arises as a consequence of the preceding variety having gone on to the squamous stage and assumed a warty appearance, due to the hypertrophy of the papillæ.

(4) The fourth variety of scratches, dermatitis gangrænosa, gangrenous, or necrotic scratches, gangrenous grease, called "Brandmauke" by the Germans, has been shown by Bang, Hell,[15] and others to own a specific cause. Commencing as a mere erythema, by lack of rest and from further exposure to the original causal influences, the affection takes on the eczematous character. In the abraded surface, coated with a greasy exudate, by mixing with which the dirt has made an air-tight packing, *B. necrophorus* finds an attractive nidus, whence it institutes its caseonecrotic process, which is always marked by a progressive character. In the progress of this destructive in-

flammation not only the skin is affected, but the subcutaneous tissue is also involved. It quite often penetrates into the tendon sheath of the flexor apparatus, causing its necrosis. The necrosis may travel upward as far as the back, involving the subcutaneous structures in that region, or it may burrow downward into the hoof structures, attacking not only the soft parts of the hoof, but also the lateral cartilages and the coffinbone. Recognizing manure and manure-contaminated soil as a secondary and frequent habitat of the necrosis bacillus, it is needless to descant on the necessity of absolute cleanliness—surgical cleanliness—of all cases, even mild cases of scratches, and the importance of promoting rapid healing.

Necrotic pox.—Smallpox of man and sheeppox are at present considered independent diseases, from either of which the pox (variola) of other animals—horses, cattle, goats, hogs—may originate. So far as the skin lesions of variola are concerned they run essentially the same course, however derived or wherever they may occur. The stages of the eruption are the papular, the vesicular, and the pustular. As a general thing the eruptions are separate, forming the so-called discrete variety. In the severer forms of the disease we may have several pocks running together to form one large pustule, forming the so-called variola confluens, or there may be present a marked petechial condition, hemorrhages into the skin, and mucous membranes occurring even before the papules make their appearance (purpura variolosa), or the pustules may become the seat of severe hemorrhage (variola pustulosa hemorrhagica). The eruptions in these severer varieties frequently progress to that stage of inflammation to which we have referred as necrotic or gangrenous, spoken of by the Germans as variola diphtherica, Brandpocke—gangrenous pox—or, on account of the horrible odor exhaled, Aaspocke—putrid pox. From gangrenous pocks in cows and sows, Bang has recovered *B. necrophorus*, and therefore regards gangrenous or necrotic pox as dependent upon this agent of necrosis. To those acquainted with the ubiquity of this bacterium, the ease with which such infection might occur is strongly confirmatory of this view. Since horses, sheep, and goats are susceptible to the necrosis bacillus, the possibility that the cause of necrotic pox in these animals is identical with that of necrotic pox in cows and sows may well be kept in mind. The present view that horsepox and cowpox originate most frequently from contact with smallpox or its congener, vaccinia, lends interest to the fact that as regards contact with the hand of man the pastern region of the horse is the analogue of the cow's udder. Hence it is likely that some cases of pox in the horse may pass for gangrenous scratches, or grease.

Jensen has described the occurrence in hogs of a necrotic dermatitis due to *B. necrophorus* and located on the muzzle, on the outside of

the lips, and on the feet. Moreover, Leclainche and Vallée [30] have made an unedited observation regarding enzootic necrosis of the lips and nose of sheep from which they recovered *B. necrophorus*. The process advanced until it completely destroyed the lips, making the prehension of food so difficult that death was caused by inanition. In addition, Bang's demonstration of this organism in the deep necroses of the skin of hogs in hog cholera has been confirmed by the findings of such investigators as Lindqvist [21] and Zschokke [41].

NECROBACILLOSIS IN RABBITS.

Four forms of this infection have been reported. In the cases cited by Mazzanti [22] and Schmorl the disease began on the lower lip and gradually involved the lower portions of the head, neck, and breast, the animals dying in about eight days.

A second type reported is characterized by abscesses in different parts of the body—thigh, flank, abdomen. They consist of fibrous sacs, showing no tendency to open, and exuding on puncture a thick, creamy, homogeneous fluid which contains the necrosis bacillus. Emaciation and death complete the disease picture.

The third variety observed presents itself under the form of necrotic dermatitis of different regions of the body. The most frequent phase generally involved the nose and upper lip and was marked by a progressive destruction of tissue reaching to the gums and nasal cavities. In other cases the hind legs and the vicinity of the genital organs became the seat of infection.

Horne [17], in his work on necrosis of the hoof in reindeer, mentions briefly the receipt at the laboratory of a dead rabbit, which on post-mortem revealed multiple necrosis of the lungs due to *B. necrophorus*.

NECROBACILLOSIS IN GUINEA PIGS.

Most authors pronounce the guinea pig almost, if not quite, immune. They generally add, however, that, if infected at all, it is by association of the necrosis bacillus with some pyogenic micro-organism. Remembering that *B. necrophorus* operates only on injured tissues, it may be assumed that the guinea pig, being less susceptible than many other animals, requires for its reception of the necrosis bacillus a more severe disturbance of tissue integrity. Again, it may be that the pyogenic organism affects some chemical alteration which lessens the normal resistance of the guinea pig. The two varieties of infection by *B. necrophorus* noticed below should settle all doubt as to the absolute immunity of the guinea pig. In 1885 Eberth [8] described a bacillary necrosis of the liver occurring spontaneously in a guinea pig. His description of the necrotic foci, the line of demarcation between healthy and diseased tissue, the rod forms

and filaments found in large numbers at the periphery, though rarely in the center of the necrotic foci, tallies closely with the well-known features of necrobacillosis of the liver in cattle and other animals and gives sufficient grounds for the statement of Birch-Hirschfeld [2] that Eberth's necrosis bacillus is practically identical with that of Bang.

The second variety has already been referred to in the introduction to this section and may be regarded as similar in type to the second form noticed under "Rabbits."

NECROBACILLOSIS OF THE HOOF.

The more intimate the association of tissues the more difficult it becomes to consider their diseases separately. This is the case in a remarkable degree in the hoof, where we find dermal and subdermal connective and muscular tissues, tendons, ligaments, and cartilages more or less tightly compressed between such unyielding substances as the bones of the hoof internally, and the horny box externally. Simple inflammations, to say nothing of more malignant forms, are rarely limited to the tissue in which they originate. Note how quickly a cutaneous quittor may become a tendinous or cartilaginous quittor, a subhorny quittor cease to be limited to the part immediately below the coronary band and involve the fleshy leaves, thus becoming a more general pododermatitis, or the bone become affected in any of these conditions. The character and limitations of this article forbid such an extensive study of necrobacillosis of the tissues of the hoof as would be required by the separate review of each.[36] The observations of Bang, Eberlein,[7] Fröhner,[12] Gutenäcker,[14] Jensen, McFadyean, and others prove that in the disastrous consequences frequently of such apparently slight injuries as nail in the foot, in all four forms of quittor, in many cases of specific necrotic pododermatitis, which are really cases of canker, in numerous cases of suppurating corn, of necrosis of the coffinbone, of phlegmonous conditions of the frog, we have to do with the presence of *B. necrophorus*.

Necrotic quittor.—In cartilaginous quittor we find the typical instance of necrobacillosis of cartilage. This, as well as the other three forms of quittor, may sometimes arise as a primary necrosis due to some direct injury, such as tread, nail prick, or heavy blow which may puncture or crush the cartilage, the instrument of injury becoming the vehicle of the infectious material. They all may be termed necrotic quittor when the necrosis bacillus is found to be present in the lesions. This condition is first manifested by an inflammation of the tissues, which results in a hot, painful swelling of the coronet over the affected quarter and marked lameness. Finally one opening—or several—appears in the swelling, which discharges a pale yellow or sanious fetid fluid. and which connects with the necrosing

cartilage by means of fistulous tracts. The wall of the hoof below the diseased quarter, stimulated to overproduction by the inflammation present, becomes thick, irregular, and grooved. When treatment is not applied, the disease usually spreads to the ligaments, joints, or even the bones, but an appropriate operation or free drainage, with the injection of strong antiseptic solutions, renders the prognosis very favorable.

Further instances of necrosis of cartilage have occurred in the course of necrotic stomatitis where the disease involves the larynx; and quite frequently in hogs, the cartilages of the nose.

As shown in our review of hoof lesions, even the bone tissue is not exempt from the destructive workings of the necrosis bacillus. All of the varieties of the hoof necroses dependent on this organism are on record as having in some instances involved the bone of the foot. Necrosis of the upper and lower bones of the jaw and even of the vertebræ has been reported in association with necrotic stomatitis. It is worthy of note that Cadiot has reported a case of necrosis of the turbinated bones in the horse, a bacteriological examination of the pus at the necropsy revealing not only streptococci and staphylococci, but also *B. necrophorus*.

NECROBACILLOSIS OF THE DIGESTIVE TRACT.

Caseonecrosis of the esophagus has been observed in both the circumscribed and diffuse forms. It has often occurred as a secondary infection in necrotic stomatitis of calves, adult cattle, and hogs by extension, in these cases frequently involving the whole length of the esophagus (Bang and Jensen). All four stomachs of ruminants have been affected with necrobacillosis. Olt [33] has seen the first three stomachs of a calf thus involved, the necrotic inflammation by its extension producing a peritonitis. He has also found in the paunches of two deer necrotic patches dependent on the presence of *B. necrophorus*, while Jensen has observed the same condition in the rumen of an antelope. Like lesions have been demonstrated in the stomachs of hogs. Necrobacillosis of the intestines has not only been observed in the intestines of cattle affected with necrotic stomatitis, but Bang has also found it in connection with an epizootic among calves in the spring of 1888. The symptom-complex of the latter disease was that of white scour, and the sick animals generally died in a few days. The necropsy in such cases revealed hemorrhages and erosions in the stomach and a diffuse catarrh of the intestine, but no areas of coagulation necrosis. On the other hand, in those cases which ran a long course there were discovered scattered over the intestinal mucous membrane patches of cheesy necrosis, in the periphery of which were demonstrated the bundles of filaments of

B. necrophorus. Just here a few words on proximal and remote causes may be in order. While recognizing the importance of the remote cause, it is to the proximal cause that we give credit for instituting the disease process under consideration. For instance, in necrotic stomatitis the proximal cause is *B. necrophorus;* the remote cause may be the eruption of the first teeth. Note here that the proximal cause is invariable, the remote variable, for, instead of being the eruption of teeth, it may be a sharp-pointed particle of food. Again, the origin of cartilaginous quittor may be nail in the foot, tread, scratches, etc. It is a variable source. But when by our histologic and bacteriologic investigation we find the necrosis bacillus associated with this caseonecrotic process, we are warranted in laying hold of that microorganism as the proximal cause—the cause which gives title to the disease process or which, on the other hand, may receive its name from the disease. So in necrobacillosis of the intestines in calves. The immediate cause of the caseonecrosis is the everywhere-present necrosis bacillus. The remote cause may be any bacterial agent capable of injuring the mucous membrane or chemical effects connected with the food—anything, for that matter, that could produce a catarrhal or eroded condition of the intestinal mucosa.

Necrobacillosis of the colon in the horse has been reported by Bang and of the cecum and colon by Olt. In hogs such caseonecrotic inflammation has been found in the small intestine, cecum, colon, and rectum [Kitt [19]]. Such lesions are not in the least surprising when we recall that *B. necrophorus* has been demonstrated to be an inhabitant of the normal intestine of healthy hogs, and that its invasion of tissue is always secondary to some disturbance of tissue integrity. We would remind the reader of Jensen's experiments regarding white scour in calves. Believing that the organism that is responsible for the disease inhabited normally the intestines of calves and waited only a break in the continuity of the intestinal mucous membrane in order to manifest its pathogenic properties, Jensen fed healthy calves with irritating chemicals and had the satisfaction of seeing them sicken with white scour; and after their death he was able to recover from blood and organs the accused bacillus. While expressing no opinion on the subject, we deem it of interest in this connection to mention the claims of Guiart concerning the etiology of typhoid fever. This observer, while not doubting the claims of *B. typhosus* as the cause of typhoid fever, considers the tricocephalus and other intestinal helminths as lancets of inoculation, the intestinal abrasions caused by them giving entrance not only to the bacillus of typhoid fever, but also to the bacterial agents of dysentery and cholera.

PARASITISM AND NECROBACILLOSIS.

The above is very neatly confirmed by an intestinal lesion in the hog usually regarded as of slight clinical importance. We refer to the cheesy follicles produced by the *Echinorhynchus gigas*. This parasite is an intestinal round worm, infesting preferably the duodenum, to the walls of which it attaches itself by the curved hooks on its proboscis. At the point where it buries itself in the mucous membrane or muscular coat of the intestine there is developed a pea-sized caseous nodule, having the armed head of the worm as its center. Olt,[31] by both microscopic examination of the nodules and inoculation of the cheesy material into rabbits, demonstrated the presence of *B. necrophorus* as the cause of the cheesy degeneration. In this laboratory the same demonstration was made with material forwarded from different abattoirs. The cheesy follicles inoculated into the back of rabbits gave rise to the caseonecrotic lesions characteristic of *B. necrophorus*. Pure cultures from the necrosed material of the rabbits proved as virulent as any derived from necrotic stomatitis of calves or hogs, demonstrated by the rapid development of anovulvitis in a cow.

NECROTIC STOMATITIS.

This is an acute, specific, highly contagious inflammation of the mouth, occurring enzootically in many species of animals, chiefly in calves, lambs, and pigs, and characterized locally by the formation of ulcers and caseonecrotic patches and by constitutional symptoms, chiefly toxic. The disease in calves is also called calf diphtheria, gangrenous stomatitis, malignant stomatitis, and, in pigs and lambs, sore mouth, canker, and ulcerative stomatitis. Necrotic stomatitis of pigs seems not to be infrequent in this country,[27] and reports of its occurrence in the Western, Southern, and Central Northern States have reached this office. Calves have shown the disease in Colorado, Texas, South Dakota, and Wyoming, but no case of the malady in lambs has as yet been brought to our attention. Dammann, Löffler, and Diem, however, have reported its occurrence among lambs in Germany, and it is not improbable that the disease is present in this country and only awaits diagnosis.

Necrotic stomatitis is both a local and a systemic affection. Primarily it is local. The local lesion is the caseonecrotic patch or ulcer, developed as a result of the multiplication of the bacilli at the point of inoculation. The general affection is an intoxication or poisoning of the whole system, produced by a soluble toxin elaborated by the bacilli.

The stage of incubation is from three to five days. Animals have shown signs of the disease when only 3 days old. During this stage

the animal organism is passive and manifests no symptoms. The stage of invasion is twofold—local reaction against the invading organisms and constitutional manifestations of intoxication. The first symptoms noted are disinclination to take nourishment and some drooling from the mouth. An examination of the mouth at this time may show on the mucous membrane of the tongue, hard palate, cheeks, gums, lips, or fauces a circumscribed area of infiltration and redness, possibly an erosion. The latter gradually extends in size and depth, forming a sharply circumscribed or at times a diffuse area of ulceration. It may measure anywhere from the size of a nickel to that of a silver dollar or even larger. It has the appearance of a corroded surface, under which the mucous membrane or lingual tissue seems transformed into a dry, finely granular, or firm cloddy mass. It is grayish yellow in color, and is bordered by a zone of thickened tissue, slightly reddened and somewhat granulated. The necrotic tissue is very adherent and can be only partially peeled off. It is homogeneous, cheesy, and may extend to the depth of 1 inch into the underlying tissue, involving the muscular tissue or even the bones. The general symptoms are languor, weakness, and slight fever. In spite of plenty of good food, the animal is seen to be failing. It stops sucking, or, if older than a suckling, altogether refuses to eat. The temperature at this time may be from 104° to 107° F. The slobber becomes profuse, swallowing very difficult, opening of the mouth quite painful, and a most offensive odor is exhaled. The tongue is swollen and its motion greatly impaired. Sometimes the mouth is kept open, permitting the tumefied tongue to protrude. One or more of the above symptoms direct the attention to the mouth as the seat of disease; or, having noticed the debility and disinclination to eat, an examination of the animal may show a lump under the neck or swelling of the throat or face as a result of the large partially chewed boluses of food that have collected there.

The general affection at this time manifests itself by dejectedness, extreme weakness and emaciation, constant lying down, with stiffness and marked difficulty in standing.

The disease frequently extends to the nasal cavities, producing a thin yellowish or greenish yellow sticky discharge which adheres closely to the borders of the nostrils. Their edges also show caseous patches similar to those in the mouth. Sometimes the nasal passage is obstructed by great masses of the necrosed exudate, thus causing extreme difficulty in breathing. When the caseous process involves the larynx and trachea, there result cough, wheezing, and dyspnea, together with a yellowish mucopurulent saliva. When life is prolonged three or four weeks caseous foci may be established in the lung, giving rise to all the signs of a broncho-pneumonia. Many of

these cases are associated with a fibrinous pleurisy. The invasion of the gastrointestinal tract is announced by diarrheic symptoms.

Ordinarily animals affected with necrotic stomatitis show no tendency to spontaneous cure. Left to themselves, they either die or become permanently stunted in growth. On the contrary, if taken in hand early, the disease is readily amenable to treatment. In the latter event the prognosis is excellent, and under favorable conditions recovery takes place as a rule in twelve to fifteen days.

ULCERATIVE ANOVULVITIS.

This is an infective enzootic of cattle affecting the tissues of the anus, vulva, and adjacent structures, and characterized by the formation of ulcers and more or less loss of tissue. The disease—also called infective ulcerative vulvitis, infectious ulcer of vulva of cattle, infectious vulvar disease, and contagious vulvitis—principally affects the young animals of a herd, and females more than males. The malady was first observed in 1898 in several States of the Central West, and does not appear to be known outside of this country. In heifers and cows the infection usually occurs on the lower portion of the lips of the vulva and in the region of the anus, while in steers it is found around the anus and root of the tail, in some cases involving the gluteal muscles. The disease has not thus far been reported in bulls. The affection is first manifested by a small inflammatory swelling on the inferior portion of the lip of the vulva, on the anus, or on the adjacent skin. The color rapidly fades and the tissue softens, forming an abrasion the size of a pin-head. The erosion spreads rapidly, and frequently several such areas become confluent, forming large phagadenic ulcers of considerable depth, containing grayish yellow or brownish colored débris of necrosed tissue covering a red granulated surface and surrounded by an irregular hemorrhagic zone. This necrosed tissue sloughs off, the secretions being yellowish in color and of a very offensive odor. Although the ulcer may scab over it will, if untreated, continue to spread under the scab and involve large patches of tissue extending deeply into the vulva and adjacent structures, in some cases producing marked deformity of the parts. During the progress of the disease there may be elevation of temperature, loss of appetite, constipation, general appearance of lassitude, and a straddling gait of the hind legs. In a small percentage of cases, usually those that have not been treated, the ulcerations progress to such an extent that death results. In the large majority of animals the disease runs a mild course, lasting from two to five weeks. The period of incubation has been reported by Repp [37] to be from a week to ten days. He cites the apparent contagiousness of the disease by describing healthy animals which after admission to an infected herd took the disease,

and premises which had previously harbored diseased animals as having produced the affection in cattle subsequently placed there. Thus the contagion seems to be confined to certain farms. Our experiments with the disease were made chiefly with tissues received from two outbreaks, one in Western Kansas, investigated by Dr. R. P. Steddom [40], the other at the Pittsburg stock yard among Western cattle. From both of these lots culture inoculations were made and the greatest amount of work was conducted upon a short motile ærobic bacillus, which seemed to be found more profusely than any other organism, but which failed to reproduce the disease when inoculated into sheep and calves. Another organism, long, beaded, and filamentous, was observed which quickly died out on ordinary culture media. From its morphologic character, from its behavior on culture media, and from its position in sections of the diseased tissue it is evident that the germ was *B. necrophorus*. A culture of this organism obtained from the intestine of a hog was injected into the lower portion of the external lip of the vulva of a cow and produced a large edematous swelling which soon ruptured and formed an irregular angry-looking ulcer, from which we concluded that this organism, which was likewise recovered from the suppurating lesion, plays an important part in the causation of the disease. The nature of the affection, its enzootic character, and its amenability to treatment are all in perfect accord with this view, which is further confirmed by the following experiment made by Steddom:

A heifer calf born in the stalk fields on January 1 was placed immediately in an infected pen and kept there for two days, after which it was returned to the stalk fields with the milch cows. Five days later the vulva became affected and remained ulcerated until January 24, when the calf passed from observation.

There is at present no satisfactory explanation for the peculiar predilection of the organism for this region. The fact that the disease has often been observed where hogs have followed cattle in the feed lot gave rise to the assumption that the former bit the cattle in the region of the tail to cause them to rise when lying down, thus making an injury which readily became infected by manure; but other outbreaks have been noted where hogs were not present and therefore could not be considered as factors in the production of the disease. The possibility of its existing secondarily to necrotic vaginitis suggests itself, but has not been demonstrated.

NECROTIC VAGINITIS.

A somewhat similar disease to the above, but one which has not been observed in this country, is the infectious necrotic vaginitis described by Ellinger. This disease has been observed in certain parts of Ger-

many and in Italy as an enzootic among cattle usually from three to eight days after calving. It is characterized by tumefaction and reddening of the vulva, the formation of ulcers and caseonecrotic patches on the mucous membrane of the vagina, and by an excessive vaginal discharge, at first serous, but later grayish and of an offensive odor. Fever and anorexia are present, the urine is passed at frequent intervals, and vaginal contractions are noticed. From the lesions of the vaginal secretions Ellinger has succeeded in isolating *B. necrophorus*, and concludes that the modification which takes place in the vagina at parturition exposes it to the causative bacillus that may be present in the manure, bedding, or on the hands of the obstetrician or his instruments. This writer also states that it is often observed with a coexisting outbreak of foot-rot of cattle on the same premises. The course of the disease is from three to four weeks, and where uterine complications are absent the prognosis is generally favorable.

NECROTIC METRITIS.

This disease is really a complication of the foregoing and results from the preexisting disease in the vagina spreading by continuity of structure to the mucosa of the uterus. The lesions observed are similar to those seen in the vagina and consist in swelling and injection of the mucous membrane, followed by erosions and sloughing of the mucosa. The uterine cavity is distended by a serosanguinolent fluid containing flocculi and shreds of necrosed tissue and becoming very malodorous. The ulceration may extend to the muscular walls of the uterus and petechial hemorrhages may be observed on the serous membranes of the body, together with enteritis, injection of the spleen, and other indications of septicemia. In some of these cases necrotic lesions of the anus and rectum have been observed, suggestive of anovulvitis, in this country, as well as of the urethra, ureters, and kidneys. The symptoms manifested are those described for necrotic vaginitis, but are more accentuated. There is evidence of much pain, the fever increases rapidly, coma comes on, and the animal dies. The course of this affection is rapid and the prognosis grave.

FOOT-ROT OF CATTLE.

A variety of causes has been ascribed for this affection, and it is probable that many of them are important agents in reducing the vitality of the parts for the subsequent invasion of the necrosis bacillus. In two outbreaks of this disease, which is also termed foul in the foot, panaritium, and panaris, we have been able to isolate *B. necrophorus* and to prove its identity by cultural and animal experiments. One outbreak, brought to our attention through the kindness of Dr. S. H. Johnston, occurred at Ambler, Pa., among a herd of

registered Guernsey cows recently imported from England. About 30 per cent of the animals showed evidence of the disease. Three years before the same disease was likewise imported from England by this breeder with another consignment of Guernseys, but no investigations of the lesions were made at that time. The second herd affected with the disease, and from which the necrosis bacillus was recovered, was located at Rochester, N. Y., and the material for examination was forwarded through the courtesy of Dr. W. O. Marshall, milk inspector of Rochester. This affection has long been recognized by the Germans as being contagious and as caused by *B. necrophorus*. Thus Bang,[1] Hess,[16] Von Imminger, and others have studied numerous outbreaks of the disease caused by the entrance of this bacillus after some primary injury to the part. It has generally been considered in this country as a filth disease, though some have held that it was contagious, owing to its spread to other cattle in the same herd, but heretofore the necrosis bacillus has not been isolated from the affected feet. Its contagious character is further indicated by the fact that the disease has been reported in this country as a forerunner of necrotic stomatitis of calves and as coexisting with necrotic vaginitis and metritis in certain parts of Germany. The symptoms of foot-rot are brought to one's attention by the apparently sudden lameness of the animal. On examination the hoof will be found to be hot, swollen, and very painful. The toes of the hoof are usually widely separated in consequence of the swelling, and frequently the tissue of the interdigital space is softened and ulcerated. The swelling may extend up the leg almost to the knee as the result of the necrotic process extending into the deeper tissues, forming fistulous tracts, abscesses, and ulcerative patches about the heel and pastern. The pus may burrow under the horn, involving the ligaments, tendons, and even the bones in its necrotic progress. The disease usually affects two or more feet of an animal, showing predilection for the hind legs. The course of the affection depends on the time when the treatment is first started. It usually lasts from five to six weeks, or even longer when the condition is neglected until far advanced. In such cases the animal becomes so lame that it remains lying all the time, appetite is lost, milk secretion suppressed, emaciation marked, fever is present, and death follows from absorption of the toxic products.

FOOT-ROT OF SHEEP.

A disease similar to the foregoing, but which does not have such a marked tendency toward extension up the leg and formation of fistulous tracts, is foot-rot in sheep. This affection has been recently studied in this laboratory,[28] with the result that *B. necrophorus* was for the first time proved to have an etiologic relationship to the

disease. The first evidence of foot-rot is a slight moisture of the interdigital membrane, which is soon associated with reddening and erosions, particularly near the heel. The inflammation rapidly progresses, forming ulcerations, from which exudes a thin purulent fluid of a characteristic pungent odor. Lameness then becomes marked, and the region of the foot above the hoof appears swollen and painful. Fistulous tracts form beneath the horny wall of the foot, which later cause loosening of the horny tissue and sometimes necrosis of the ligaments and adjacent structures. In the chronic form of the disease the continued irritation of the bacteria causes a development of fungoid growth, while the hoof of the sheep grows out rapidly, becoming hard with thickened and elongated claws which curl up like sled runners. Walking may become so painful that the sheep lies down continuously; the temperature rises, appetite is decreased, and the animal rapidly becomes emaciated. The prognosis is very favorable when treatment is applied in the early stages of the disease, a cure resulting within ten days. It is very rare for death to occur as a result of foot-rot, although in virulent outbreaks involving three or all four feet of each sheep the affection may terminate fatally within two months.

Horne has described the disease as it occurs in reindeer and succeeded in proving the necrosis bacillus to be the etiologic factor.

NECROTIC OMPHALOPHLEBITIS.

This disease is found among young animals and consists of an inflammatory condition with firm swelling of the navel and the surrounding tissues. Later this swollen mass, which is hot and painful, rapidly softens in the center, undergoing suppuration and necrosis. The necrotic process causes an irregular cavity at this point, which may reach the size of a silver dollar and is associated with a sanious, fetid discharge. The general symptoms are fever, loss of appetite, diarrhea, and occasionally death. Microscopic examination of the necrosed tissue from the umbilicus and inoculation experiments have shown, in the hands of McFadyean,[23] Jensen,[18] Olt, and others, that *B. necrophorus* is the causative agent. The difference between this affection and similar diseases produced by infection of the umbilicus with pyogenic cocci, or the organism of white scours, is one only of degree, as in the former case the necrosis and consequent cavity formation are more marked and there is a greater tendency toward complication of the joints, with bone necrosis, as will be referred to below, or to necrotic stomatitis, resulting from the calf licking the diseased navel and infecting the mucous membrane of the mouth, a method of infection which has been observed by Mettam [24] in a number of calves.

JOINT-ILL.

This disease, also called joint-evil, is not infrequent among young animals, especially calves and foals, and occurs within six weeks after birth. The disease is localized in the joints, but the infection may reach the liver or other viscera, causing small areas of necrosis. One or more joints may be involved, a condition manifested by local painful swellings. The animal is stiff and lame and lies down most of the time, showing fever, inappetence, and accelerated respiration. The joint cavity is filled with pus, which finally causes ulceration of the cartilage and even necrosis of the adjoining bone. In the purulent material of the joint *B. necrophorus* has been found by Mettam [25] and others, who claim that the disease starts in such cases by infection of the umbilicus with the necrosis bacilli. Of course, it is not to be presumed that all cases of joint-ill are caused by this organism, since it has been proved definitely that the pus-producing cocci and the bacillus of white scour may enter the unhealed umbilicus and be carried by the umbilical vein to the liver, where they are thrown into the circulation to become localized in one or more joints. But the very fact that this does not occur in the latter cases presupposes the probability of the same occurrence with *B. necrophorus*.

MULTIPLE NECROSIS IN LIVER, LUNGS, AND OTHER VISCERA.

Among the first lesions in which *B. necrophorus* was recognized in this laboratory were necrotic nodules in the liver of a deer which died at the National Zoological Park and in livers of cattle shipped to this office by the meat inspection force at Kansas City and Chicago in 1900 for diagnosis. The organism had evidently been observed at an earlier date by Theobald Smith in the intestinal ulcerations of hog cholera, as has been shown above, but it was not until the last two years that the bacillus was recovered and studied in pure culture in this laboratory.

The livers above mentioned were somewhat enlarged in size and presented on the surface and sometimes within their parenchyma a number of necrotic areas of varying sizes from a grain of wheat to a walnut, sharply delimited from the apparently healthy tissue adjacent. These nodules were usually firm in consistency, of a greenish or grayish-yellow color, irregularly rounded in outline, and extending like an infarct into the normal tissue. On the border line between the normal and diseased tissue numerous columns of necrosis bacilli may be observed on microscopic examination, but not in the center of the dead tissue.

Later the areas of necrosis become circumscribed by dense fibrous capsules, while the contents are softened and changed into a greenish-yellow pus. The number of these areas in the liver is variable, most

frequently from ten to twenty, and, as a rule, they approach a hickory nut in size. McFadyean has reported their occurrence not only in the liver of cattle, but also of sheep [a] and in the lungs of horses. In the latter cases the nodules are about the same size though softer in consistency than in the liver, sometimes containing thick grayish-yellow pus in the center. They occasionally reach the size of a goose egg and the pleura over the necrosed areas becomes thickened and gelatinous. Multiple areas of necrosis have also been reported by Bang in the muscles of the heart, which in one case was embolic, and in the other case of traumatic origin. Such lesions as have been described as occurring in the liver, lungs, and heart of animals are not suspected during life, since no symptoms referable to them have been observed. The first knowledge that such lesions exist is obtained by postmortem examination. Whereas multiple necrosis of the liver of cattle is not infrequently seen by meat inspectors in their postmortem work, such animals on antemortem examination do not reveal the least evidence of these lesions. The most interesting feature connected with this condition is the possible paths of infection of this bacillus. It has been concluded by McFadyean that, in certain cases observed by him, an external lesion of the hock or superficial sloughing of the skin was the point of entrance of the germ. In those cases in which no such ulcerating surfaces are present it is presumed that the bacillus enters the alimentary canal and reaches the portal circulation, whence it is disseminated throughout the liver with resulting areas of necrosis. It is also possible, as Ostertag,[35] Edelmann,[9] Olt,[32] and Meyer [26] have suggested, for these organisms to reach the liver through the umbilical vein by infection of the navel. It is not unlikely that following the healing of the navel these centers of infection in the liver remain as the only result of such omphalic contamination, and hence on slaughter no other lesions may be observed in the carcass. The foci in the lungs and cardiac necrosis can be readily explained as of embolic origin from the bacilli circulating in the blood. Thus Nielsen [29] described two cases of pulmonary necrosis in horses following scratches, and Caudwell [3] a similar case. The latter observer had previously reported one case of multiple necrosis in the lung of a calf, in which the lesions were metastatic and secondary to an ulcerative patch on the palate of the animal, and similar necrotic areas in the heart, kidney, and voluntary muscles of cattle.

Jensen and Georgewitsch [13] have likewise reported bacillary necrosis in the kidneys as well as in the spleen of cattle.

[a] Although McFadyean has not furnished satisfactory proof for this assertion, the fact that bacillary necrosis does occur in the liver of sheep has been determined by the experiments of Mettam [25] and Edelmann,[9] the latter also observing it in the liver of hogs, horses, and dogs.

HOG CHOLERA AND NECROBACILLOSIS.

There can be no doubt that hitherto the hog-cholera bacillus has been given too much credit for the lesions customarily seen in that disease. As long ago as 1887 it was surmised by Schütz, and demonstrated in 1889 by Bang and later confirmed by Zschokke, Olt,[84] and others that the superficial necroses occurring in the intestine and stomach of cases of hog cholera were due to the hog-cholera bacillus, whereas the deeper necroses were invariably dependent upon the presence of *B. necrophorus* playing, as secondary invader, its rôle of producer of deep and progressive tissue necrosis.

This view is still further confirmed in our minds by a recent study of a number of histological preparations belonging to this laboratory and made by Prof. Theobald Smith during the investigation of hog cholera in the eighties. Slide No. 19, dated October, 1884, marked "Hog cholera, ulcer of the stomach," number of pig not given, reveals superficial ulcer, great numbers of micrococci, and short rods. On the other hand, sections of ulcers of stomach from pigs Nos. 125, 140, and 145 show ulcers penetrating deeply into the submucosa. At the base of these ulcers is to be seen a deeply stained ribbon made up of bundles of long filamentous bacilli enveloping in their meshes numerous round cells and leucocytes. Between this line and the still sound portion of the intestinal wall is an area of poorly stained cells bespeaking in all probability the incipient necrosis produced by the toxin of the advancing necrosis bacilli. Slides from intestinal ulcers and ulcers of the colon of pigs Nos. 67, 71, 72, 73, and 121 all show the superficial portions of the necrosed intestinal wall crowded with micrococci and short rods, but in the deeper portions of the ulcers penetrating the loose connective tissue structure of the submucosa are to be found invariably the long, wavy, beaded filaments so characteristic of *B. necrophorus*.

As additional evidence we refer to recent examinations made by us of caseonecrotic lesions in hogs just dead of hog cholera. In all such chronic lesions, whether of the stomach or intestine, we found in the deeper portions on the border line between the healthy and diseased tissues numerous bundles of *B. necrophorus*. Inoculation of such material into the back of a rabbit resulted in the usual coagulation necrosis, bearing out the statement of Theobald Smith that "in rabbits the local effect of such inoculation is usually quite severe."

AVIAN DIPHTHERIA AND NECROBACILLOSIS.

It must be acknowledged that the final word on the etiology of so-called avian diphtheria has not yet been spoken. Till then the specificity of the disease is open to question. The almost universal acknowledgment that the word "diphtheria" should be associated only with

the Klebs-Löffler bacillus makes the title "avian diphtheria" a misnomer for the affections usually so denominated. It is admitted on all sides that various microorganisms possess the power of producing diphtheric inflammations—that is, inflammations characterized by the production of a membrane. The several microorganisms, more or less pathogenic, sometimes in pure culture, recovered by different investigators from various outbreaks of pseudomembranous inflammations of the mouth and throat of chickens and other avian species speak loudly in favor of this position. The failure of equally able men to recover from equally virulent outbreaks the same microorganism is still further confirmatory. In numerous necropsies of different species of birds affected with exudative and pseudomembranous inflammations of the mouth, nose, and throat we have been struck with the decided tendency toward localization of the lesions in those regions, the failure to recover any organism from the blood, and the enforced inference of death from toxinemia. Some recent bacteriologic findings in this laboratory have increased the importance of these observations. From the exudate in the mouth of the kite, to which reference has already been made, was recovered by cultural and animal inoculation methods a pathogenic variety of *Bacterium ærogenes* together with *Bacillus necrophorus*. From two chickens affected with diphtheritic roup and representing different flocks and different outbreaks was recovered, by cultural and animal inoculation methods, *B. necrophorus*. In the case of one chicken there was also associated a nonmotile rod pathogenic for rabbits; in the other a nonpathogenic organism was associated with the necrosis bacillus. The bacteria above mentioned were in neither case pathogenic for chickens nor were lesions produced by the injection of *B. necrophorus*. It is more than a mere inference—in fact, it is a logical deduction—when we assume that the local depredations of associated bacteria or other irritating agent offered to the soil- and manure-contaminating necrosis bacillus a ready entrance into the tissues as a secondary invader.

We do not consider that we have settled the question of avian diphtheria. We do wish the name could be abolished and for such affections in the avian species titles be used that are more in accord with the pathologic findings. Remembering that Ritter found the necrosis bacillus in association with what he called avian diphtheria, that Jensen has lately recorded some unpublished investigations by his assistant Leth in the same line, we suggest deep-going local antiseptics in the treatment of all pseudomembranous affections of the mouths of chickens and other birds, and at the necropsies of all fatal cases of such affections careful search for *B. necrophorus*.

EXPERIMENTAL PATHOLOGY.

Inoculation experiments are an important aid in diagnosis. The tissue changes in the rabbit and mouse after inoculation with *B. necrophorus* are so characteristic as to become an essential factor in the identification of the microorganism. Furthermore, the work of recovering the necrosis bacillus is much simplified by the use of these animals.

EXPERIMENTS ON RABBITS.

Subcutaneous method.—These animals are highly susceptible to the action of *B. necrophorus*, and to this susceptibility is due the ease with which the presence of the germ in diseased tissue may be demonstrated. A bit of tissue adjacent to the border of the necrosed area is emulsified in a normal saline solution. The subcutaneous inoculation of a rabbit with 0.5 c. c. of this emulsion will result in the death of the animal within one week. In order to free the tissues of the experiment animal from other forms of microorganisms naturally present in material taken from a necrotic area in contact with the outside world, it is advisable to use a second or even a third rabbit. The first rabbit will, however, in spite of the contaminated material used in its inoculation, show very characteristic lesions, which can be referred to the action of no organism other than the bacillus of necrosis. The chief of these typical changes will be noted at the point of inoculation, where, lying beneath the skin and extending down for a greater or less depth into the muscular tissues, is found an irregular area about 1½ to 2 inches in diameter. This area offers to the naked eye much the appearance of a flattened mass of soft, fresh putty, and to the nose the penetrating odor already referred to as between the smell of cheese and that of glue. This pulpy, yellowish-white malodorous mass is the detritus of muscular, fatty, and vascular tissues which have been attacked and destroyed through the presence of the necrosis bacillus as well as by its effective poisons. Reaching out into the surrounding tissues for about 1½ inches in all directions is found a zone of inflammatory tissue, and the subcutaneous and muscular tissues of the abdominal region are inflamed and edematous through extension by gravitation of the disease process from the local lesion caused by inoculation. Not seldom in these cases is there to be observed a marked development of gas bubbles. Frequently that portion of the large colon adjacent to the diseased abdominal wall is greatly injected and adherent to the parietal peritoneum by a plastic exudate containing numerous short and long forms of the bacillus of necrosis. This part of the peritoneum is also inflamed and presents petechial hemorrhages. Examination of the soft mass found in the necrosed area at the point of inoculation shows that it is penetrated

in every direction by long threadlike bacilli, and the subcutaneous inoculation of a second rabbit with a small scraping from this mass serves to eliminate a large proportion of the contaminating organisms. Because of the greater purity of the material now used, the inoculation will not result fatally until a period usually from eight to fourteen days, although occasionally death has been deferred nineteen, and in one case twenty-three, days. In many instances it will be found that this longer period has proved sufficient to allow the circulation to take up a few of the bacilli and deposit them in the plexuses of the lungs, liver, or kidneys, where small, yellowish-white spots of necrosis will result, which may be readily peeled out as if in a capsule.

From these secondary visceral necroses pure cultures of *B. necrophorus* may now be obtained, and its further development secured by the utilization of anaerobic methods of culture. The injection of 0.5 c. c. of these pure cultures under the skin of the back produced the same characteristic yellowish-white area of muscular necrosis about the point of inoculation and the peculiar penetrating odor so constant with this bacillus. The course of the disease is about the same as when an emulsion of the fresh tissue has been injected, and in those cases in which life was prolonged several weeks metastatic areas of focal necrosis were always noted. The approach of death is usually indicated by convulsions; the animal comes out of one to be seized with another, death generally resulting in a few hours after the onset of the first convulsion. In the majority of rabbits that succumbed to this disease a marked rigor mortis was observed, especially noticeable in the hind quarters, causing the back to be arched and the legs contracted as if in a tetanic spasm. Microscopic examination of tissue taken from the necrosed area or from metastatic lesions of the liver or lungs shows the presence of typical necrosis bacilli in great numbers. In the case of organic lesions these filaments are seen to be arranged along the border of the area of necrosis, whereas the central portion is amorphous and does not reveal the presence of any microorganisms.

Intravenous method.—The intravenous method of inoculation was adopted in nine cases, four of which resulted in the death of the animal. Each rabbit received in the posterior auricular vein 0.3 c. c. of an emulsion of the tissue filtered through cotton, the filtrate containing numerous bacilli.

The course of the disease ranged from seven to twelve days. The symptoms exhibited in all cases were the same as those induced by subcutaneous inoculation, and consisted of gradual emaciation, followed by the loss of appetite and by convulsions, paralysis, and death. The postmortem examination showed the principal lesions to be

located in the thoracic cavity. The lungs contained several caseous nodules the size of peas surrounded by a hemorrhagic zone, and in one rabbit the left principal lobe was adherent to the costal pleura by a thick, purulent exudate. In each case the costal pleura contained several metastatic foci, and the chest muscles in two instances were the seat of one or two localized areas of coagulation necrosis. In another the caseous process had included the entire surface of both lungs, the pericardium, and the heart itself, until all were superficially fused into one cheesy mass. The liver of one animal contained eight superficial areas of caseation varying in size from a pea to a hazelnut and was adherent to the diaphragm and abdominal muscles. All other organs were normal. No lesion was observed about the point of inoculation in three cases; the fourth showed a narrow strip of necrosis along the line of the vein for about half an inch. Cover-glass preparations made from the lesions contained numerous characteristic specimens of *B. necrophorus*.

EXPERIMENTS ON MICE.

Subcutaneous inoculation.—The remarkable susceptibility of the white mouse to "necrophorus infection" makes this animal an excellent medium for the preservation of the virulence of that microorganism, as well as a means of obtaining it in pure culture. Unfortunately, this animal's extreme susceptibility to many forms of bacteria usually found in necrotic areas disqualifies it for use in the early stages of an investigation. The inoculation experiments may be carried on by placing a small bit of necrosed tissue in a pocket in the skin of the back, or by injecting into the same region 0.1 c. c. of a fluid culture or emulsion containing the germ in a pure state. In two to four days the point of inoculation is covered with a rather thick, blackish, or dark-brown dry scab, around which is a zone of redness. Beneath this scab proceeds a coagulation necrosis spreading through the subcutaneous tissues until the mouse is completely mummified, shriveled up, and covered with a dry parchment-like coating; or, penetrating into the body cavities in its course, successfully caseates muscle, cartilage, bone, and viscera. In some of these cases so general becomes the caseous process that it is difficult to decide whether the viscera have suffered embolic necrosis or have become involved in the progressive caseation through extension by contiguity. In cases in which necrotic action was less widespread small focal necroses containing *B. necrophorus* in pure culture were found in the lungs, liver, and spleen. In our experiments mice have died as early as five and as late as twenty-one days.

EXPERIMENTS ON GUINEA PIGS.

Guinea pigs were inoculated with pure cultures of necrosis bacilli by both the subcutaneous and intraabdominal methods, but these were followed by negative results. Nine animals were used in the experiments, and doses ranging from 0.25 to 1 c. c. of a forty-eight hour bouillon culture were injected without producing any unfavorable effects. However, one positive result was obtained in guinea pig No. 3181, which was injected intraabdominally with 0.5 c. c. of an emulsion of the necrosed tissue taken from the mouth of a calf. Death followed on the tenth day. On autopsy the carcass appeared emaciated. The point of inoculation in the prepubic region was surrounded by an abscess several millimeters in diameter containing a rich yellowish pus. In the linea alba, several inches above this abscess, was an extensive nodule 1.5 cm. in diameter, involving the muscular tissue and the peritoneal lining. It contained the same character of pus. On the right side of the linea alba the peritoneum was adherent to the contiguous loop of the colon opposite the last rib. The right and left lobes of the liver were almost fused into one by abscess formation. The right lobe particularly was the seat of several abscesses 1½ cm. long by 1 cm. wide, with a line of demarcation plain and straight between the part absolutely necrosed and the invaded portion. The spleen appeared mottled and slightly enlarged, and the kidneys were deeply congested. The lungs were engorged on the right side and showed one or two foci of hepatization. The presence of *B. necrophorus* in these liver abscesses was demonstrated by microscopic preparations and by animal inoculations.

GENERAL PROPHYLAXIS.

Prophylaxis should be carried out in various ways, according to the particular character of necrobacillosis to be prevented. Thus joint-ill, omphalophlebitis, and such cases of multiple necrosis of the liver and other viscera as arise from infection of the umbilicus may be prevented by the following precautionary measures: The female, at the end of the period of gestation, is provided with dry, clean bedding and comfortable quarters. The external genitals and tail are washed with 3 per cent creolin or lysol solution. Immediately after the birth of the young its umbilical cord is cleansed and disinfected by an application of the same solution, followed by painting it with flexible collodion, or a solution composed of 1 pint of wood alcohol and 15 grains of iodine. By this treatment the navel is rid of contaminating organisms, and the exposed blood vessels at that point are closed as paths of infection.

Again, in necrotic stomatitis, prevention would consist in the thor-

ough disinfection once daily for five days of the mouths and nostrils of those animals that have been exposed by the eruption of the first teeth or by the shedding of the milk teeth or through association with affected animals. In preventing necrotic quittor and scratches it is necessary to take all wounds and injuries of the hoof early and treat them antiseptically to prevent their contamination with the necrosis bacillus. To avoid necrotic vaginitis absolute cleanliness should accompany all treatment of obstetrical cases and prompt repair be made of all lacerations and other injuries of the genital tract following parturition. In all forms of necrobacillosis it is essential to separate the sick from the healthy animals, and to disinfect completely all stalls, sheds, pens, etc., with a 5 per cent solution of carbolic acid, to which has been added sufficient lime to make the disinfected area conspicuous. As it has been shown that the large majority of species of domestic animals are susceptible to this infection and that a constant relation may exist between an attack of one form of necrobacillosis and the previous occurrence of another type of the infection in the same or another species of animal on the place, it behooves one to prevent any susceptible animal of whatever species from coming in contact with a diseased one, or with such stalls, sheds, manure, and old bedding as might be harborers of the contagion.

GENERAL THERAPEUTICS.

In those cases of necrobacillosis with external lesions the treatment consists, first, in removing the caseous patches or necrotic tissue in order to expose the causative agent. The latter being an anaerobe, exposure to the atmosphere will of itself prove beneficial. Removal of the necrosed material may be accomplished by the use of a curet, knife, or hot iron. The exposed area should then be treated as a common wound by washing it thoroughly with antiseptic solutions, especially Lugol's solution or 5 per cent carbolic acid, which seem to have a greater effect on the bacillus than most germicides. The formation of granulation tissue in exposed regions may be stimulated by antiseptic salve, such as carbolized vaseline, or by dressings of camphor or calomel. In necrotic quittor, where the cartilage has become involved, it is advisable to inject strong caustic solutions for the purpose of destroying the diseased tissue or to extirpate the diseased cartilage by an operation, followed by the usual antiseptic dressing. In necrotic vaginitis and metritis douches of warm antiseptic solutions, such as 1 per cent carbolic acid, creolin, or lysol, are indicated. Success has followed the treatment of anovulvitis with 5 per cent solution of carbolic acid or creolin and the subsequent application of silver nitrate to the ulcers as a caustic. The treatment of multiple necrosis of the viscera is not possible, as the symptoms are

rarely noted, and even if they were diagnosed remedies would not avail.

ECONOMICS.

This, the objective point of the paper, our readers will concede has been kept before us throughout the entire discussion. In necrobacillosis we have a many-sided affection of vast importance to the agriculturist and of considerable interest to those in control of zoological gardens. It may locate itself in any tissue. Few, if any, animals are immune from natural infection by it. Any disturbance of tissue integrity, whether by disease or traumatism, opens the way for its invasion. Its bacillary agent, *B. necrophorus*, is everywhere present, notably in manure and manure-contaminated soil.

Its presence in any part of the body is a menace to the joints and viscera by reason of its metastatic tendencies, and an almost certain harbinger of death by general intoxication. The existence of the disease in one animal endangers the growth, usefulness, and even life of every other susceptible animal on the farm. The ease with which it is grafted on a damaged tissue is equaled only by the facility with which it may be ousted by the early use of energetic antisepsis. The fact that it is enzootic instead of epizootic makes it no less costly to the farmer whose stock becomes the sphere of its operations. In short, in *B. necrophorus* and necrobacillosis we have an ever-impending danger concerning which it is not too much to aver that its presence is as common as that of manure, its inoculability as easy as that of blackleg, its financial depreciation of the individual attacked as positive as that of scabies, its fatality as high as that of foot-and-mouth disease, and its treatment as simple as that of epizootic lymphangitis. Nevertheless, the disease is not one which, like some others, the Government can by sanitary regulations proceed to eradicate. The individual farmer, aided by the weapons of veterinary science, must battle with it himself.

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